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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/004,833 | 12/07/2001 | Donald J. Buchsbaum | | 7772 |

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09/09/2005

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| EXAMINER |
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HARRIS, ALANA M

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| ART UNIT | PAPER NUMBER |
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1643

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/004,833

Applicant(s)

BUCHSBAUM, DONALD J.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-7,9,10,12 and 13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-7,9,10,12 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Applicant's election of species b (included in generic claims 1, 2, 4-7, 9, 10, 12 and 13) in the reply filed on June 22, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1, 2, 4-7, 9, 10, 12 and 13 are pending.

Claims 3, 8 and 11 have been cancelled.

Claims 1, 2, 7 and 9 have been amended.

Claims 1, 2, 4-7, 9, 10, 12 and 13 are examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2, 4-7, 9, 10, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation, "...administering, about simultaneously," in claim 1 is vague and indefinite. This language is not clearly understood and consequently the administration step cannot be precisely determined by those of ordinary skill in the art. The claims should be so clear in that one of ordinary skill in the art will clearly know

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what is being claimed.

b. The recitation "...the antibodies against a growth factor receptor..." listed in line 2 of claim 13 does not further limit from independent claims 1 and 12. Claim 1 cites antibodies to a Her-2/neu receptor. The language of claim 13 broadens the scope of the antibodies to be administered.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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6. Claims 1, 2, 4-7, 9, 10, 12 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,632,979 B2 (effective filing date March 16, 2000). U.S. patent #6,632,979 discloses HER2-directed treatments of cancers, including pancreatic and colon cancers, see column 25, lines 20-48; column 26, lines 8-32. The disclosed method treatments embody anti-Erb2 antibody therapeutic regimens combined with the coadministration of the anti-cancer agents, such as anti-ErbB2 antibodies including HERCEPTIN with chemotherapeutic agents, see column 10, lines 59-65; column 26, line 53-column 27, line 2. The therapeutic regimen may be radioisotopes, as well as the chemotherapeutic agents chosen from the list presented in Applicant's claim 4, see column 13, line 66-column 14, line 65. The therapeutic molecules are administered at an initial dose of 4 mg/kg, followed by a weekly maintenance dose of 2 mg/kg for a time period until a desired suppression of disease symptoms occurs, see column 27, lines 44-50. It is within the purview of the Examiner that this time period reads on a course of treatment of at least 6 weeks. Notwithstanding, Figures 3, 5 and 7 demonstrate the administration of HERCEPTIN with anti-cancer agents for at least 6 weeks.

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6. Claims 1, 2, 4-7, 9, 12 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number 2002/0051785 A1 (effective filing date March 20, 2000). U.S. patent application publication #2002/0051785 discloses methods that involve the use of an antibody capable of inhibiting Her-2/neu receptor function thereby inhibiting the growth of mammalian cells and treating a mammal suffering from a cancer, see sections 0012 and 0013. A number of antibodies capable of inhibiting Her-2neu receptor function can be used to inhibit cell growth including monoclonal antibody 4D5 (ATCC CRL 10463), see sections 0077, 0084, 0085, 0097, 0115 and 0116. This growth inhibition reads on both, *in vitro* and *in vivo* and the cancers to be treated include, colon and pancreatic cancers, see sections 0023 and 0043.

HERCEPTIN in combination with chemotherapy have proven to be effective, see section 0049. Chemotherapeutic agents disclosed in the publication are paclitaxel and cisplatin, see section 0038. The anti-cancer drug, 5-fluorouracil can also be used with the taught antibodies, see section 0119. An initial dose of about 1ug/kg to 15mg/kg can be administered with subsequent dosages within the range from about 1 ug/kg to 100mg/kg given daily thereafter for several days or longer. It is reasonable to conclude that the longer dose administration reads on at least 6 weeks, see section 0134. The taught therapies may include chemotherapies and/or radiation therapies administered concurrently or sequentially, see sections 0135, 0136 and 0138-0140.

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7. Claims 1, 2, 4, 7, 9, 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Colbern et al. (Journal of Inorganic Biochemistry 77: 117-120, 1999). Colbern discloses a method of antitumor activity in metastatic breast cancer patients with the administration of a combination therapy inclusive of STEALTH (pegylated) liposomal (PL) cisplatin or non-liposomal cisplatin and Herceptin, see abstract; page 118, sections 2.3 and 2.5 and Results section beginning on page 118. The combination therapy was given at least 6 weeks and at high doses initially then there was dose reduction, see Figures 1 and 2 on page 119; Figure 3 on page 120; and page 120, column 2, first sentence.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1, 2, 4-7, 9, 10, 12 and 13 rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication number 2002/0051785 A1 (effective filing date March 20, 2000), in view of U.S. Patent number 6,632,979 B2 (effective filing date March 16, 2000). The teachings of the patent application publication have been presented in the 102(e) rejection. The patent application publication does not teach the method using gemcitabine as the chemotherapeutic agent.

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However, patent #6,632,979 does teach the implementation of gemcitabine as a chemotherapeutic agent useful in the treatment of cancer, see column 14, lines 8, 9 and 56 and 57. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to include gemcitabine in the combined Her-2/neu receptor antibodies and chemotherapeutic treatment of pancreatic and colon cancer. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in both documents because of the successful treatment of solid tumors with a range of chemotherapeutic agents observed in both documents. Moreover, the combination of the antibodies and chemotherapeutic agents has been proven to result in significant antitumor efficacy, see both documents.

10. Claims 1, 2, 4-7, 9, 10, 12 and 13 rejected under 35 U.S.C. 103(a) as being unpatentable over Colbern et al. (Journal of Inorganic Biochemistry 77: 117-120, 1999), in view of U.S. Patent number 6,632,979 B2 (effective filing date March 16, 2000). The teachings of Colbern have been presented in the 102(b) rejection. Colbern does not teach a method of inhibiting colon or pancreatic tumor growth comprising administering antibodies to Her-2/neu receptors about simultaneously with radioisotopes and the chemotherapeutic agents, irinotecan (CPT-11), paclitaxel, 5-fluorouracil, doxorubicin and specifically gemcitabine.

However, patent #6,632,979 teaches the treatment of pancreatic and colon cancer with the combination of anti-cancer agents, HERCEPTIN and chemotherapeutic agents and/or radioisotopes, see column 13, line 66-column 15, line 7; column 25, lines

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20-48. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to implement a combined Her-2/neu receptor antibodies and chemotherapeutic/radioisotope treatment to pancreatic and colon cancer. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in the recited patent and Colbern because of the successful treatment of solid tumors with a range of anti-cancer agents observed in both documents. Moreover, the combination of the antibodies and chemotherapeutic/radioisotope agents has been proven to result in significant antitumor efficacy, see both documents.

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Safran et al. Herceptin and Gemcitabine for Metastatic Pancreatic Cancers That Overexpress HER-2/*neu*. Cancer Investigation 22(5): 706-712, 2004.; and


Mrsic et al. Trastuzumab in the treatment of advanced breast cancer: Single-center experience. Annals of Oncology 12 (Suppl. 1): S95-S96, 2001.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm with alternate Fridays off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
31 August 2005